Nager syndrome

Nager syndrome is a rare condition that mainly affects the development of the face, hands, and arms. The severity of this disorder varies among affected individuals.

Children with Nager syndrome are born with underdeveloped cheek bones (malar hypoplasia) and a very small lower jaw (micrognathia). They often have an opening in the roof of the mouth called a cleft palate. These abnormalities frequently cause feeding problems in infants with Nager syndrome. The airway is usually restricted due to the micrognathia, which can lead to life-threatening breathing problems.

People with Nager syndrome often have eyes that slant downward, absent eyelashes, and a notch in the lower eyelids called an eyelid coloboma. Many affected individuals have small or unusually formed ears, and about 60 percent have hearing loss caused by defects in the middle ear (conductive hearing loss). Nager syndrome does not affect a person's intelligence, although speech development may be delayed due to hearing impairment.

Individuals with Nager syndrome have bone abnormalities in their hands and arms. The most common abnormality is malformed or absent thumbs. Affected individuals may also have fingers that are unusually curved (clinodactyly) or fused together (syndactyly). Their forearms may be shortened due to the partial or complete absence of a bone called the radius. People with Nager syndrome sometimes have difficulty fully extending their elbows. This condition can also cause bone abnormalities in the legs and feet.

Less commonly, affected individuals have abnormalities of the heart, kidneys, genitalia, and urinary tract.

Frequency

Nager syndrome is a rare condition, although its prevalence is unknown. More than 75 cases have been reported in the medical literature.

Genetic Changes

The cause of Nager syndrome is unknown. Although the specific genes involved have not been identified, researchers believe that this condition is caused by changes in a particular region of chromosome 9 in some families.

Nager syndrome disrupts the development of structures called the first and second pharyngeal arches. The pharyngeal arches are five paired structures that form on each side of the head and neck during embryonic development. These structures develop into the bones, skin, nerves, and muscles of the head and neck. In particular, the first and second pharyngeal arches develop into the jaw, the nerves and muscles for

chewing and facial expressions, the bones in the middle ear, and the outer ear. The cause of the abnormal development of the pharyngeal arches in Nager syndrome is unknown. It is also unclear why affected individuals have bone abnormalities in their arms and legs.

Inheritance Pattern

Most cases of Nager syndrome are sporadic, which means that they occur in people with no history of the disorder in their family. Less commonly, this condition has been found to run in families. When the disorder is familial, it can have an autosomal dominant or an autosomal recessive pattern of inheritance.

Autosomal dominant inheritance means one copy of an altered gene in each cell is sufficient to cause the disorder, although no genes have been associated with Nager syndrome. In autosomal dominant Nager syndrome, an affected person usually inherits the condition from one affected parent.

Autosomal recessive inheritance means both copies of a gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of a mutated gene, but they typically do not show signs and symptoms of the condition. Nager syndrome is thought to have an autosomal recessive inheritance pattern when unaffected parents have more than one affected child.

The underlying genetic cause may differ among unrelated individuals with Nager syndrome, even among those with the same pattern of inheritance.

Other Names for This Condition

- acrofacial dysostosis 1, Nager type
- AFD1
- NAFD
- Nager acrofacial dysostosis
- Nager acrofacial dysostosis syndrome
- preaxial acrofacial dysostosis
- preaxial mandibulofacial dysostosis

Diagnosis & Management

These resources address the diagnosis or management of Nager syndrome:

- Genetic Testing Registry: Nager syndrome
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C0265245/
- University of California San Francisco Medical Center
  https://www.ucsfbenioffchildrens.org/conditions/nager_syndrome/

These resources from MedlinePlus offer information about the diagnosis and management of various health conditions:

- Diagnostic Tests
  https://medlineplus.gov/diagnostictests.html
- Drug Therapy
  https://medlineplus.gov/drugtherapy.html
- Surgery and Rehabilitation
  https://medlineplus.gov/surgeryandrehabilitation.html
- Genetic Counseling
  https://medlineplus.gov/geneticcounseling.html
- Palliative Care
  https://medlineplus.gov/palliativecare.html

Additional Information & Resources

MedlinePlus

- Encyclopedia: Cleft Lip and Palate
  https://medlineplus.gov/ency/article/001051.htm
- Encyclopedia: Hearing Loss - Infants
  https://medlineplus.gov/ency/article/007322.htm
- Health Topic: Bone Diseases
  https://medlineplus.gov/bonediseases.html
- Health Topic: Craniofacial Abnormalities
  https://medlineplus.gov/craniofacialabnormalities.html

Genetic and Rare Diseases Information Center

- Nager acrofacial dysostosis
  https://rarediseases.info.nih.gov/diseases/498/nager-acrofacial-dysostosis

Educational Resources

- Boston Children's Hospital: Congenital Limb Defects
  http://www.childrenshospital.org/conditions-and-treatments/conditions/congenital-limb-defects
- Disease InfoSearch: Nager acrofacial dysostosis
  http://www.diseaseinfosearch.org/Nager+acrofacial+dysostosis/5094
- MalaCards: acrofacial dysostosis 1, nager type
  http://www.malacards.org/card/acrofacial_dysostosis_1_nager_type

- Orphanet: Nager syndrome
  http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=245
- University of California San Francisco Medical Center
  https://www.ucsfbenioffchildrens.org/conditions/nager_syndrome/

Patient Support and Advocacy Resources

- Children's Craniofacial Association
  http://www.ccakids.org/
- Cleft Palate Foundation
  http://www.cleftline.org/
- National Organization for Rare Disorders (NORD)
  http://rarediseases.org/rare-diseases/nager-syndrome/
- Resource list from the University of Kansas Medical Center: Facial Anomalies/ Craniofacial Conditions
  http://www.kumc.edu/gec/support/craniofa.html

Genetic Testing Registry

- Nager syndrome
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C0265245/

ClinicalTrials.gov

- ClinicalTrials.gov
  https://clinicaltrials.gov/ct2/results?cond=%22Nager+syndrome%22+OR+%22Craniofacial+Dysostosis%22

Scientific articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28Craniofacial+Dysostosis%5BMAJR%5D%29+AND+%28%28nager+syndrome%5BTIAB%5D%29+OR+%28nager+acrofacial+dysostosis+syndrome%5BTIAB%5D%29+OR+%28preaxial+acrofacial+dysostosis%5BTIAB%5D%29+OR+%28nager+acrofacial+dysostosis%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D

OMIM

- ACROFACIAL DYSOSTOSIS 1, NAGER TYPE
  http://omim.org/entry/154400

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